<Bioinformatics Center> Biological Information Networks

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- Biological Information Networks -

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Visitors

CONG, Yang	The University of Hong Kong, China, 7 May–4 August 2009
Dr VERT, Jean-Philippe	Mines ParisTech and Curie Institute, France, 19 June–18 August 2009
Dr MELKMAN, Avraham	Ben Gurion University, State of Israel, 14 October 2009–5 January 2010

Scope of Research

Due to rapid progress of the genome projects, whole genome sequences of organisms ranging from bacteria to human have become available. In order to understand the meaning behind the genetic code, we have been developing algorithms and software tools for analyzing biological data based on advanced information technologies such as theory of algorithms, artificial intelligence, and machine learning. We are recently studying the following topics: systems biology, scale-free networks, protein structure prediction, inference of biological networks, chemo-informatics, discrete and stochastic methods for bioinformatics.

Research Activities (Year 2009)

Publications

Nacher JC, Hayashida M, Akutsu T: Emergence of Scale-Free Distribution in Protein-Protein Interaction Networks Based on Random Selection of Interacting Domain Pairs, *BioSystems*, **95**, 155-159 (2009).

Tamura T, Akutsu T: Algorithms for Singleton Attractor Detection in Planar and Nonplanar AND/OR Boolean Networks, *Mathematics in Computer Science*, **2**, 401-420 (2009).

Kato Y, Akutsu T, Seki H: Dynamic Programming Algorithms and Grammatical Modeling for Protein Beta-Sheet Prediction, *Journal of Computational Biology*, **16**, 945-957 (2009).

Presentations

Comparing Biological Networks via Graph Compression, Hayashida M, 3rd International Symposium on Optimization and Systems Biology (OSB 2009), 20 September 2009.

Completing Networks Using Observed Data, Tamura T, 20th International Conference on Algorithmic Learning Theory (ALT 2009), 4 October 2009.

Integer Programming-Based Methods for Attractor Detection and Control of Boolean Networks, Akutsu T, The combined 48th IEEE Conference on Decision and Control and 28th Chinese Control Conference (IEEE CDC 2009), 17 December 2009.

Grants

Akutsu T, Goto S, Mochizuki A, Tokita K, Mathematical Analysis of Structure and Dynamics of Biological Information Networks, Grant-in-Aid for Scientific Research on Priority Areas, 1 April 2005–31 March 2010.

Akutsu T, Kawabata T, Nagamochi H, Hayashida M, A Novel Approach to Computational Drug Design Based on Graph Theory and Kernel Methods, Grant-in-Aid for Scientific Research(A), 1 April 2007–31 March 2011.

Akutsu T, Data Compression Based Approach to Elucidation of Principles of Complex Biological Systems, Grant-in-Aid for Exploratory Research, 1 April 2007–31 March 2010.

Finding Minimum Reaction Cuts of Metabolic Networks under a Boolean Model Using Integer Programming and Feedback Vertex Sets

In this work, we consider the problem of, given a metabolic network, a set of source compounds and a set of target compounds, finding a minimum size reaction cut, where a Boolean model is used as a model of metabolic networks. The problem has potential applications to measurement of structural robustness of metabolic networks and detection of drug targets. We develop an integer programming based method for this optimization problem. In order to cope with cycles and reversible reactions, we further develop a novel integer programming (IP) formalization method using a feedback vertex set (FVS). When applied to an *E. coli* metabolic network consisting of Glycolysis/Glyconeogenesis, Citrate cycle and Pentose phosphate pathway obtained from KEGG database, the FVS-based method can find an optimal set of reactions to be inactivated much faster than a naive IP-based method and several times faster than a flux balance-based method. We also confirm that our proposed method works even for large networks and discuss the biological meaning of our results.

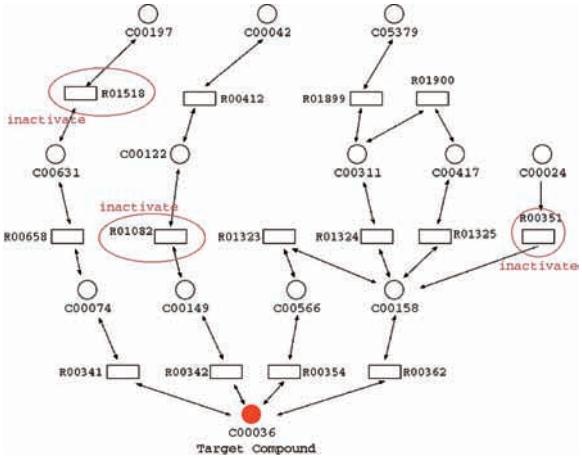

Figure 1. Relationship among the target compound and deleted reactions when C00036 is the target compound. In our computer experiment with a partial map of KEGG, deleting {R00351, R01082, R01518} effectively prevented the target compound to be produced.

Comparing Biological Networks via Graph Compression

One of the central problems in bioinformatics and systems biology is comparison of various kinds of biological data. Methods for comparison of DNA and/or protein sequences have been extensively studied and have been applied to analyses of real sequence data quite successfully. On the other hand, data compression methods have been applied to comparison of large sequence data and protein structure data. Since it is still difficult to compare global structures of large biological networks and data compression-based methods can be applied to comparison of large-scale sequence data, it is reasonable to try to apply data compression methods to comparison of biological networks.

Here, we propose a novel method for comparing biological networks. In the proposed method, an original network structure is compressed by iteratively contracting identical edges. Then, the similarity of two networks is measured by a compression ratio of the concatenated networks. The proposed method is applied to comparison of metabolic networks of *H. sapiens*, *M. musculus*, *A. thaliana*, *D. melanogaster*, *C. elegans*, *E. coli*, *S. cerevisiae*, and *B. subtilis*. The results suggest that our method can efficiently measure the similarities between metabolic networks.

Hayashida M, Akutsu T: *Lecture Notes in Operations Research*, pp. 168-176.

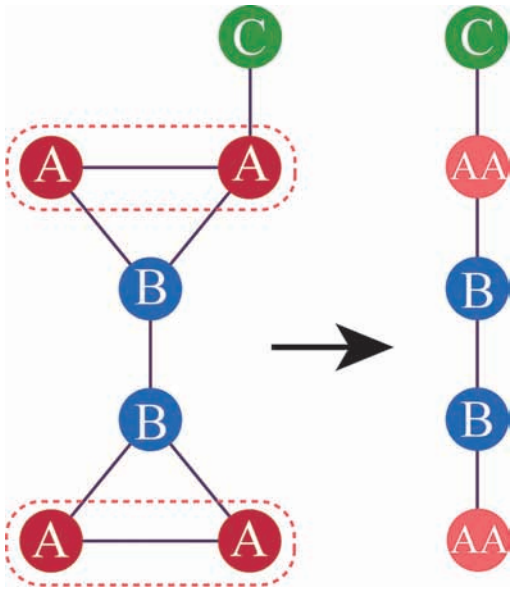

Figure 2. Example of edge contraction.

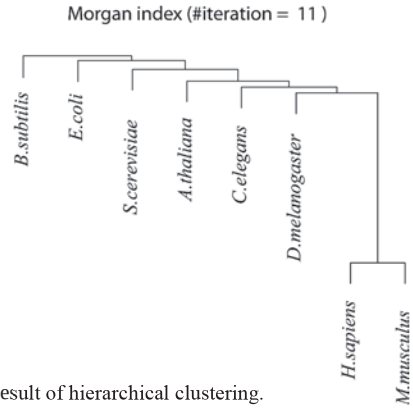

Figure 3. Result of hierarchical clustering.